2016 Fall term SyBBi Seminar Class

入門課程 III (Introductory Course III)

A short lecture on p-value and q-value

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Terminology名詞 I

- null hypothesis 空假設(虛無假設)
- alternative hypothesis 對立假設
- statistics 統計
- probability distribution 機率分佈
- standard deviation 標準誤差、標準偏差
- Central limit theorem 中央極限定理
- normal distribution 常態分佈

Null hypothesis 空假設

- No specific assumption is made on the sample.
- Sample is randomly selected
- Sample is the **control set**

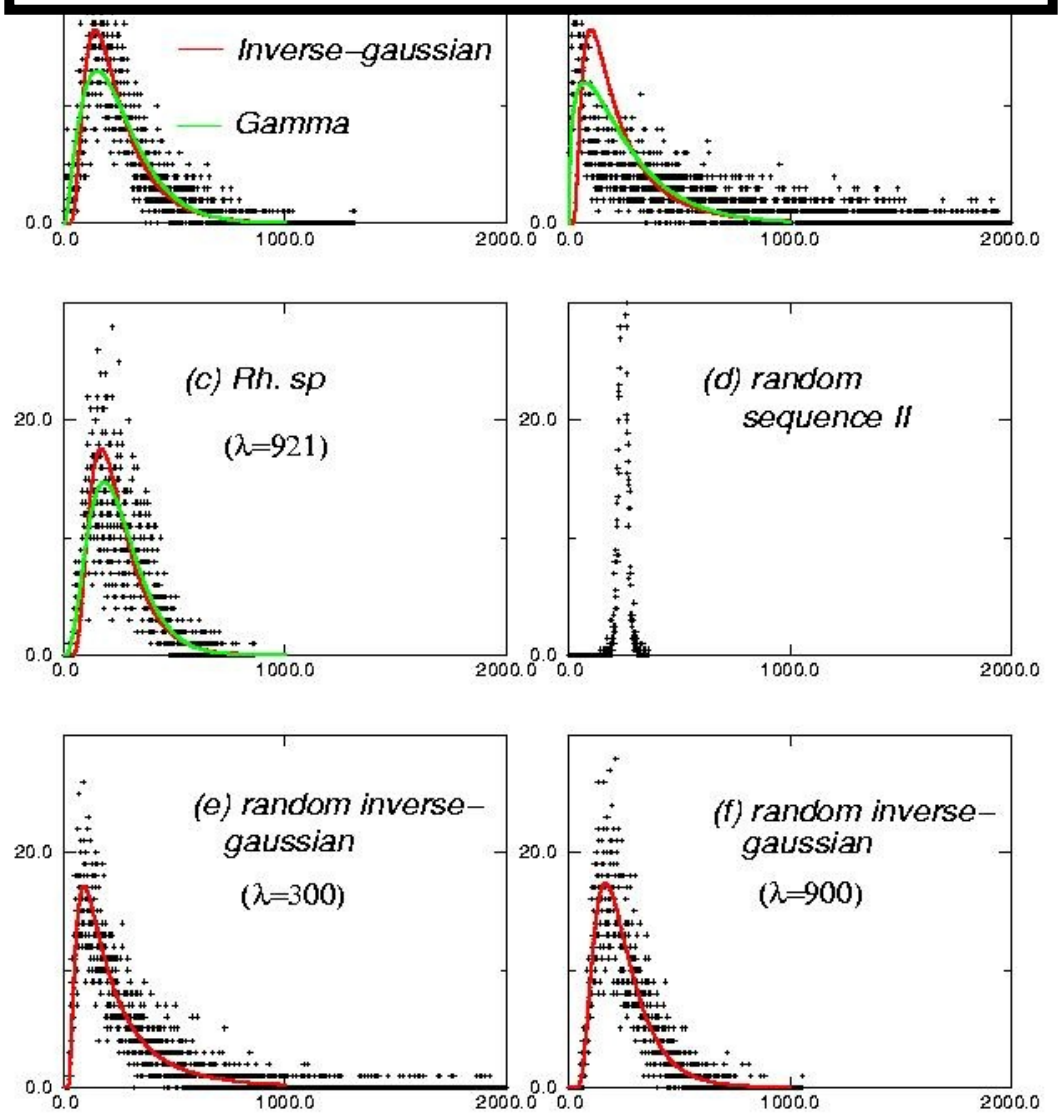
Alternative hypothesis
對立假設

- A specific assumption is made on the sample.
- Sample is NOT randomly selected
- Example: disease, genotype, phenotype, drug application
- Sample is the **test set**

Statistics 統計 & Probability distribution 機率分佈

- We are always interested (or studying) in a sample set, or a cohort 隊列
- Hence the need for statistics
- In the sample set, the property we are interested in will differ among individuals, the property will have a DISTRIBUTION of values

Some distributions

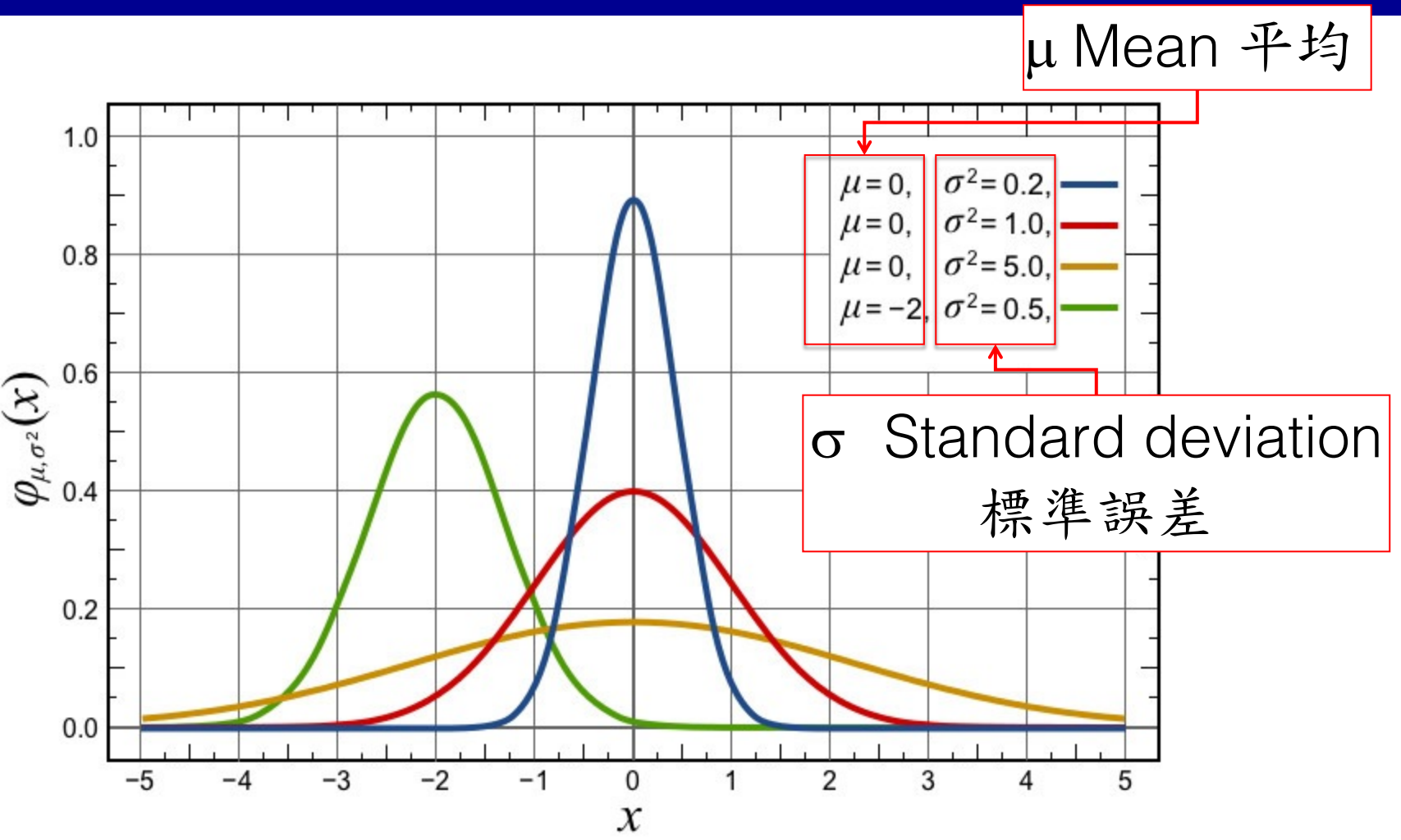


Count/quantity/prbability

Property

probability = count/total count

Central limit theorem 中央極限定理 & Normal distribution 常態分佈 (The bell curve)



Terminology 名詞 II

- Significant test 顯著測試
- population mean, m | sample mean
- SD of population, σ | SD of sample, σ
- t-test t-檢驗 | z-test z-檢驗
- p-value - false positive rate 假陽性率
- multiple simultaneous tests 多個同步測試
- standard error of the mean 平均值的標準誤差

Significant test 顯著測試

- A significant test – a test to see whether a (measured) value $\overline{X}$ can be explained by the null hypothesis H_0 (e.g., normal) that expects a value μ
- We make this test because we want to know whether the measure value $\overline{X}$ is a result of the alternative hypothesis H_a (e.g., abnormal)
- Test takes the form
  - Given expect value from H_0: μ, how significant is measured value H_a: $\overline{X}$
  - One-sided test H_a: $\overline{X} > \mu$ or H_a: $\overline{X} < \mu$
  - Two-sided test H_a: $\overline{X} \neq \mu$

Single significant test 單顯著測試
t-test and *p*-value

- t-test is expressed in terms of the t-score

  $t = (X - \mu) / \sigma$ = no. of SD's deviates from μ

- *p*-value, probability this can happen with normal distribution (variable x) with SD = σ
- One sided test
  - If H_a: $> \mu$, *p*=probability $x > \mu$
  - If H_a: $< \mu$, *p*=probability $x < \mu$
- Two-sided test
  - H_a: $\neq$ m, *p*= sum probability of $|x| > |\mu|$
- Given t-score, one can get a *p*-value from a table or a software program

Multiple simultaneous tests
多個同步測試
t-test t-檢驗 | z-test z-檢驗 (I)

- Suppose our object of study is not a single measurement, but the measurements of a sample of size n. Suppose the means of the measurements is $\overline{X}$
- To get a p-value, we can do a t-test or a z-test, depending on n and what we know about SD.

Multiple simultaneous tests 多個同步測試
t-test t-檢驗 | z-test z-檢驗 (II)

- σ: SD of population;
  s: SD* of sample. (Sample is a sub-set of population)

If (i) we do not know σ, AND (ii) n<30, we use

t-test: $t = (X - \mu)/(s/\sqrt{n})$; $s^2 = \Sigma_i(X_i - \mu)^2/(n-1)$

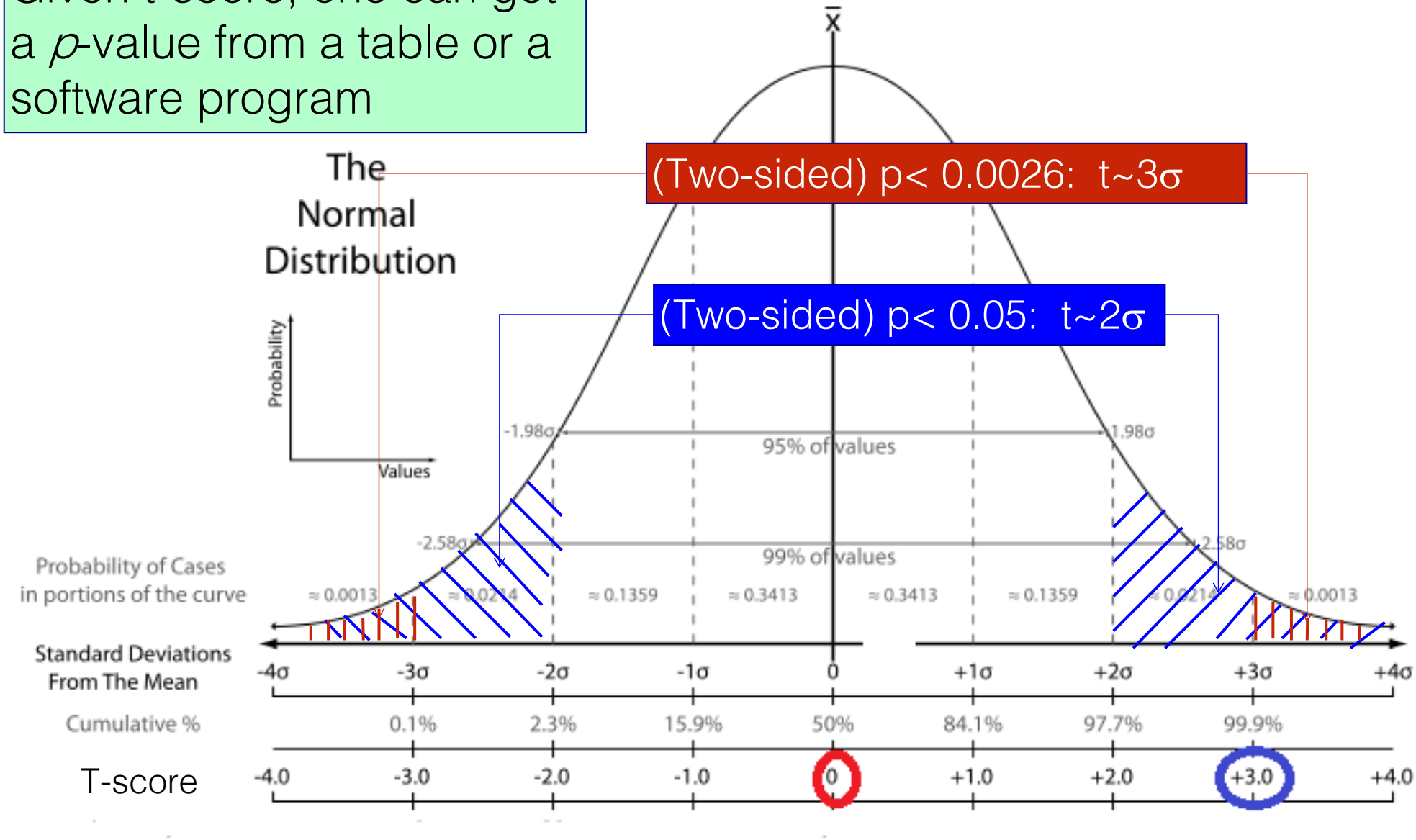
$s/\sqrt{n}$: standard error of the mean 平均值的標準誤差

- Otherwise we use

z-test: $z = (X - \mu)/(\sigma/\sqrt{n})$

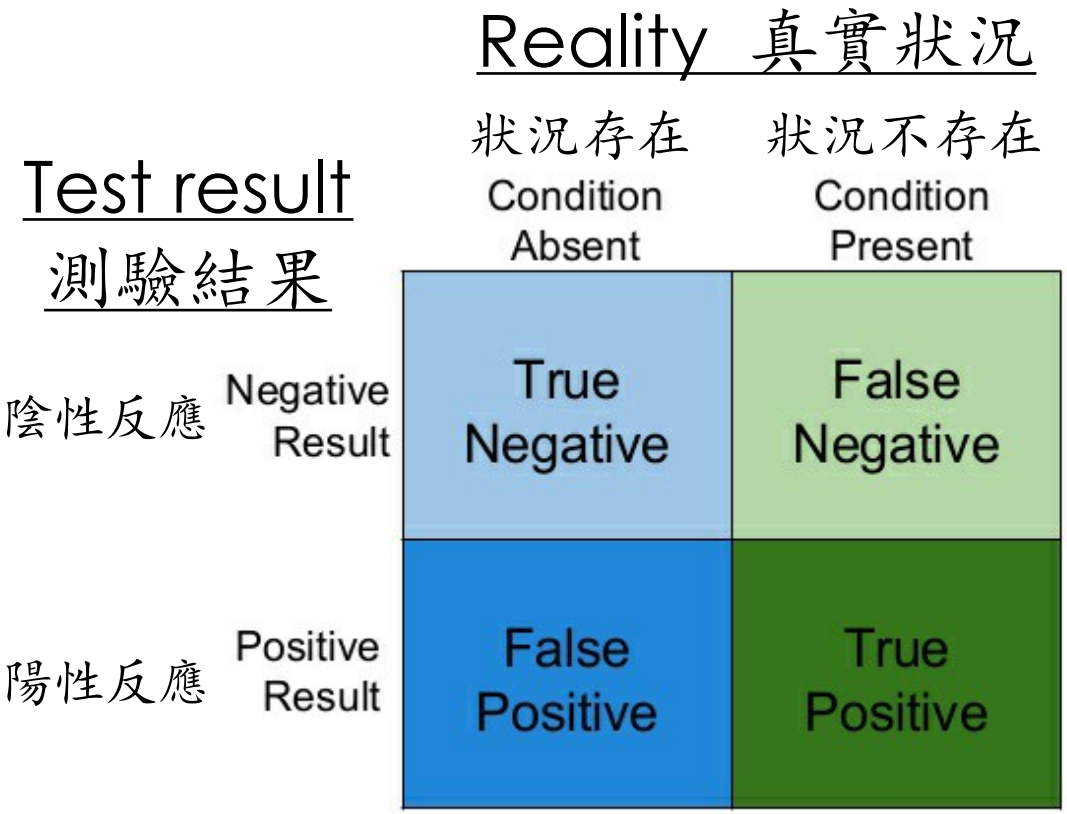
Normal distribution, SD, t-score, *p*-value

Given t-score, one can get a *p*-value from a table or a software program



http://www.statisticshowto.com/wp-content/uploads/2013/09/The_Normal_Distribution.svg_1.png

True/False 真/假
Positive/Negative 陽/陰



- True Negative – condition absent and test negative
  真陰性 – 無狀況、陰性反應
- False Negative – condition present and test negative
  假陰性 – 有狀況、陰性反應
- False Positive – condition absent and test positive
  假陽性 – 無狀況、陽性反應
- True Positive – condition present and test positive
  真陽性 –有狀況、陽性反應

- **Desired: minimize False positive and False Negative**
  理想結果：假陽性與假陰性

(Highly simplified) Blood test and lymphoma
（高度簡化的）驗血與淋巴瘤

- In a blood test various types of blood cells are counted. An elevated level of lymphocytes (a type of white blood cell) may be linked to specific lymphomas. 驗血時會測血液中各種血球的數量。如果淋巴细胞（一種白血球）數量過高可能是某種淋巴瘤導致。

- A **False Positive** is when a blood test suggests a healthy patient has lymphoma; a **False Negative** is when a blood test suggests a patient having lymphoma is healthy. 驗血判斷健康的病患有淋巴瘤謂**假陽性**，判斷有淋巴瘤的病患健康謂**假陰性**。

Terminology名詞 III

false positive rate = 假陽性率

#of false positives /#of all true null tests

false discovery rate = 錯誤發現率

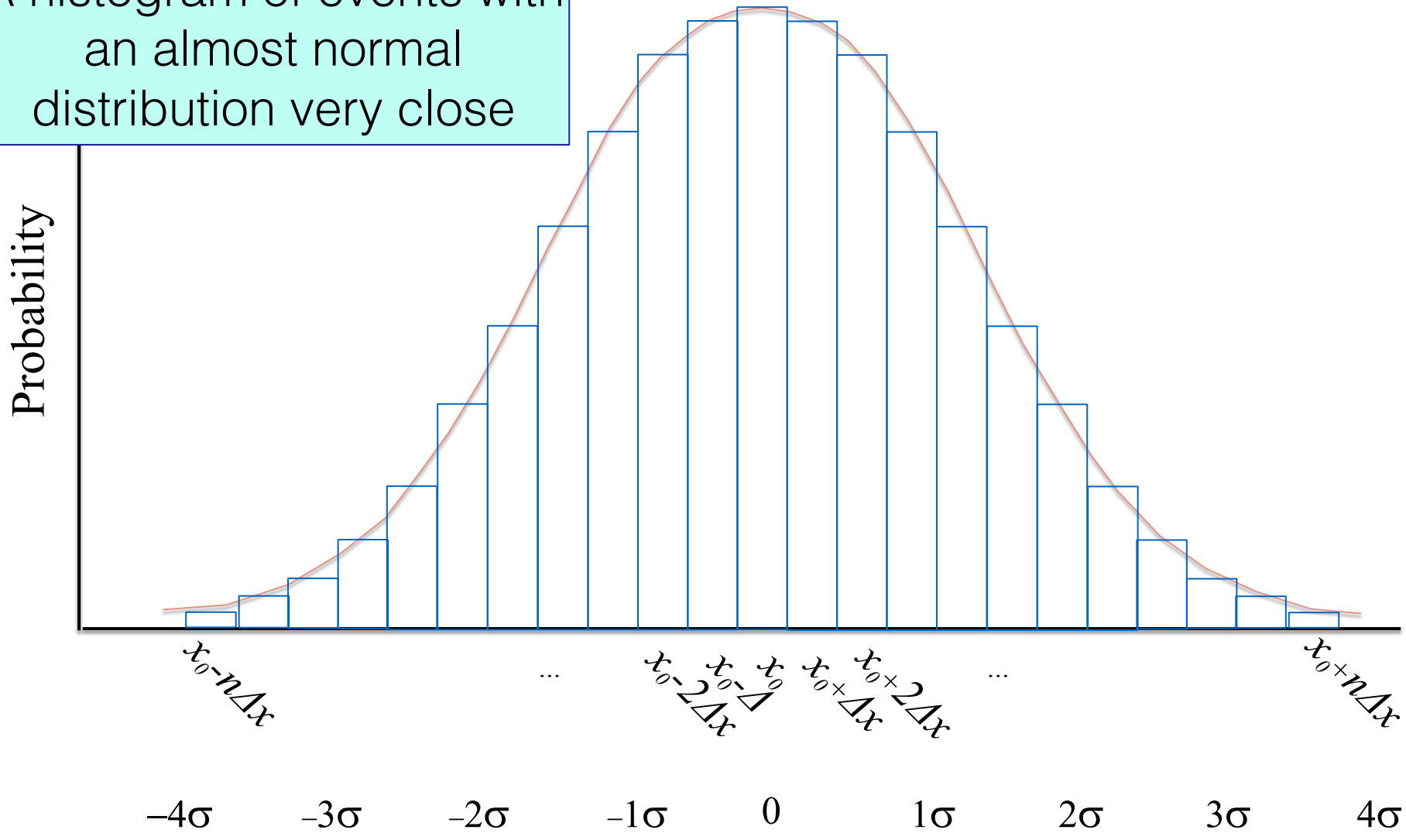
#of false positives /# of significant tests

***p*-value** – probability null hypothesis is true 空假設是真的機率 – minimum false positive rate 最低假陽率

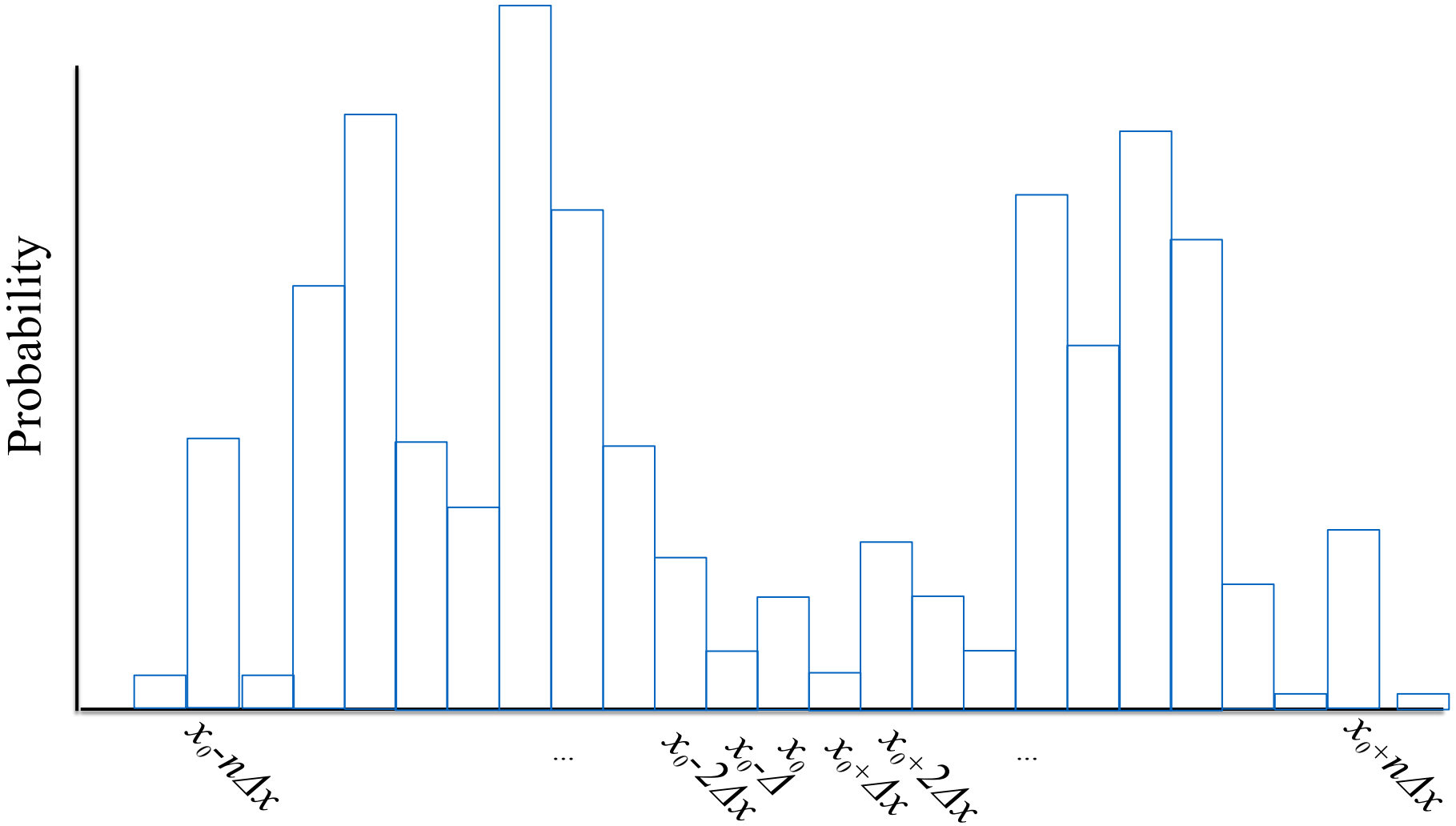
***q*-value** – minimum false discovery rate (FDR)最低錯誤發現率

A (normal) distribution - probability distribution of measure values

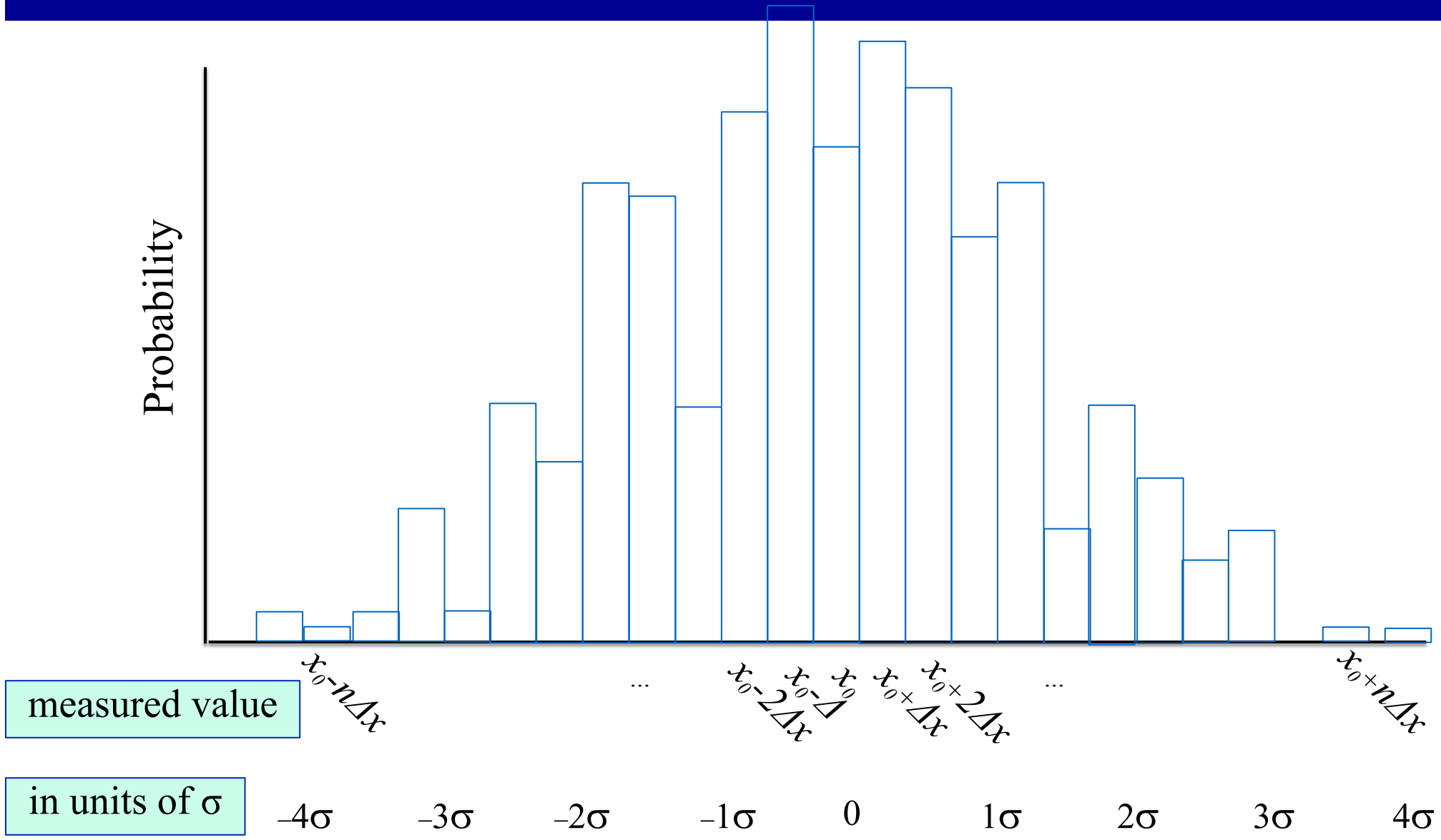
A histogram of events with an almost normal distribution very close



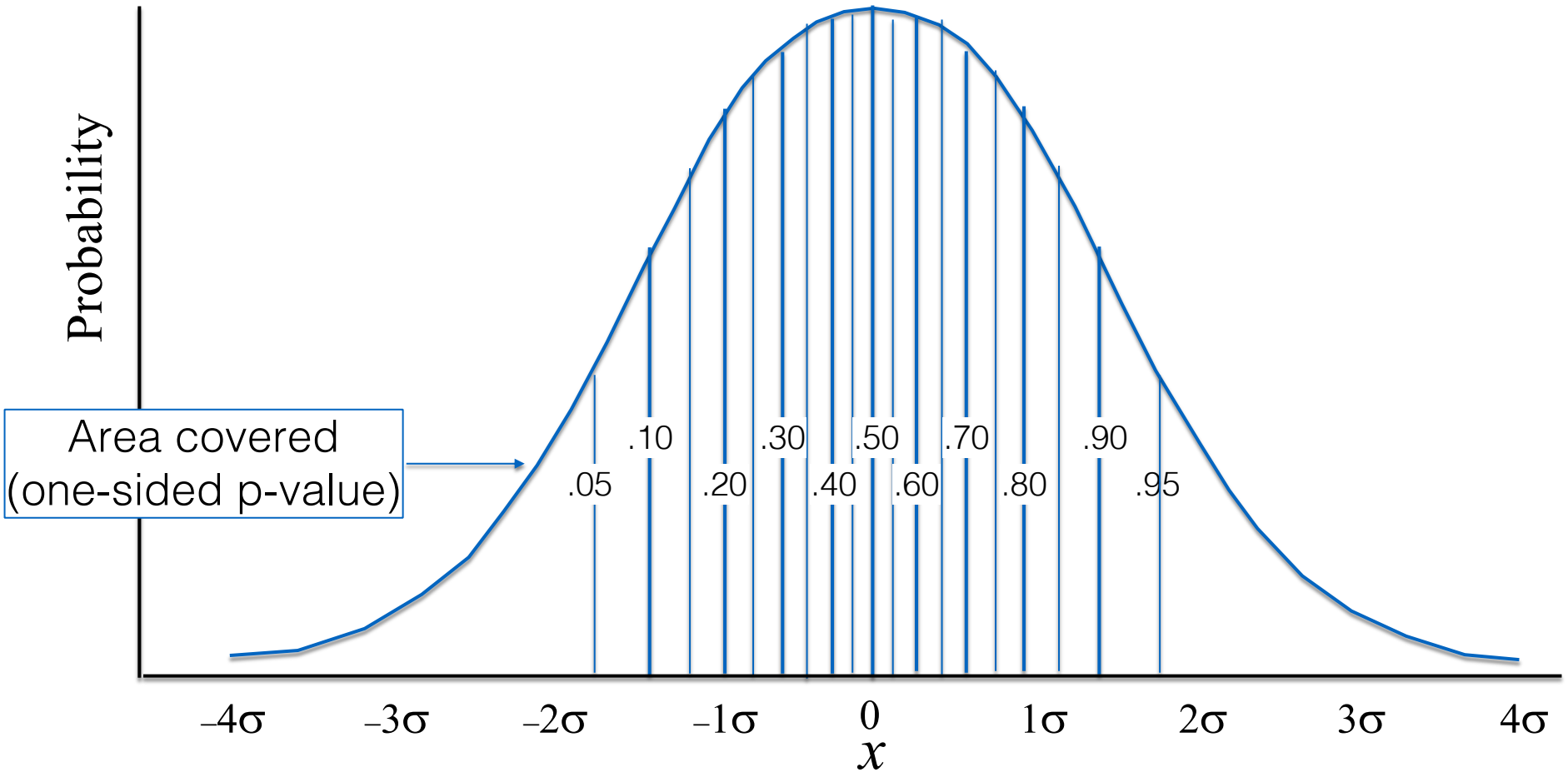
A distribution (histogram) that is far from being a normal distribution



A distribution (histogram) that is close to a normal distribution

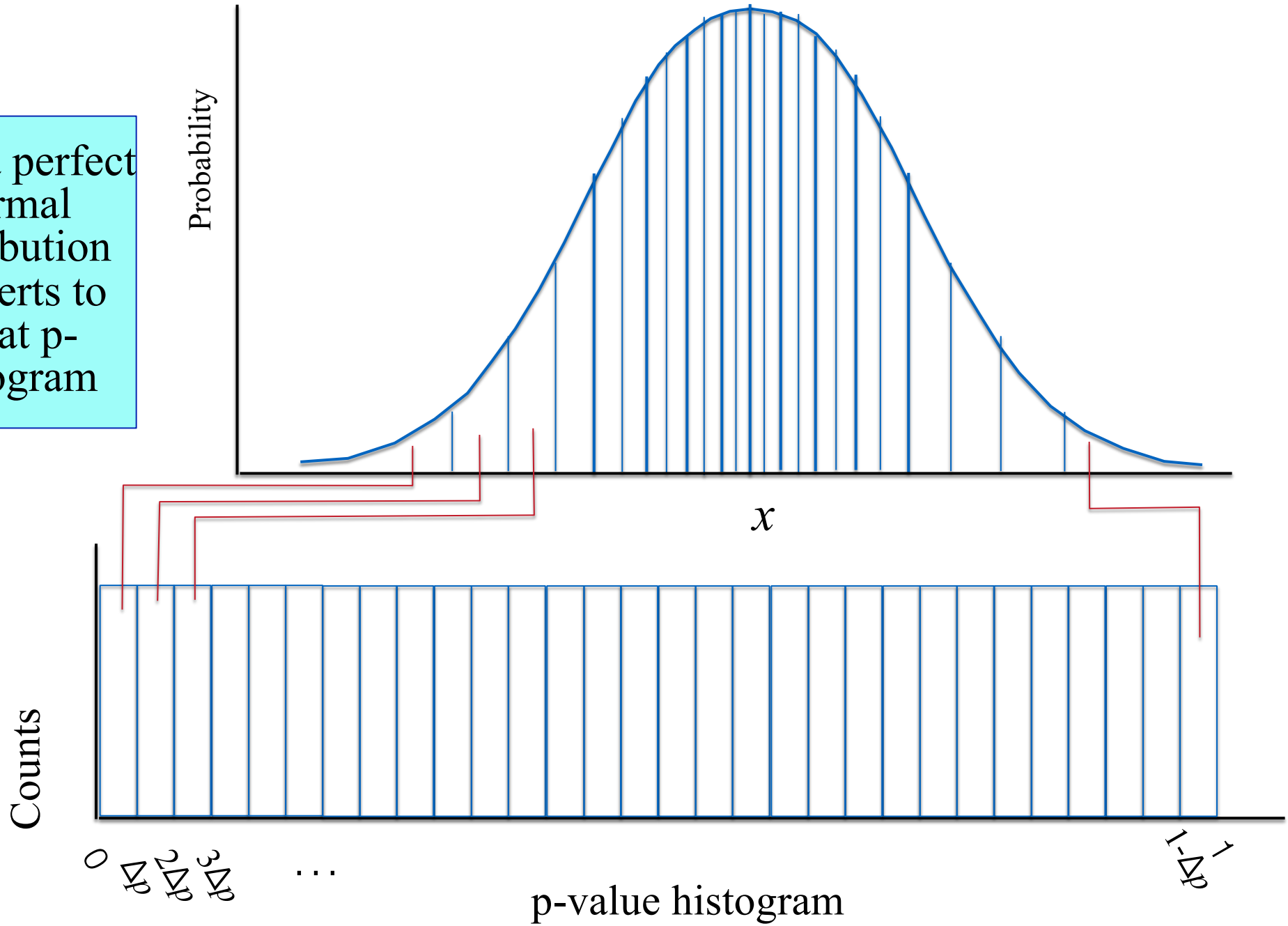


Normal distribution partitioned into equal p-value intervals



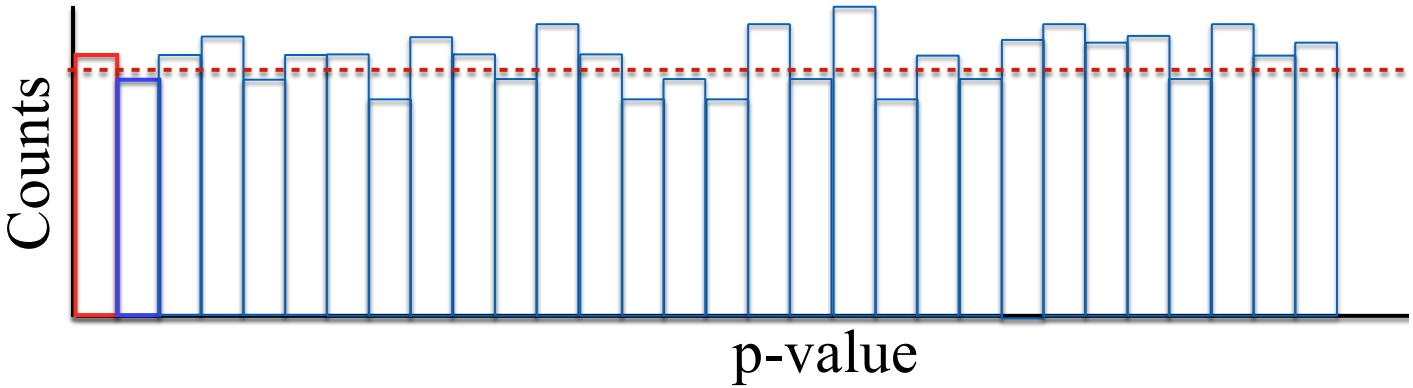
Covert an x-distribution to a p-value histogram

Only a perfect normal distribution converts to a flat p-histogram

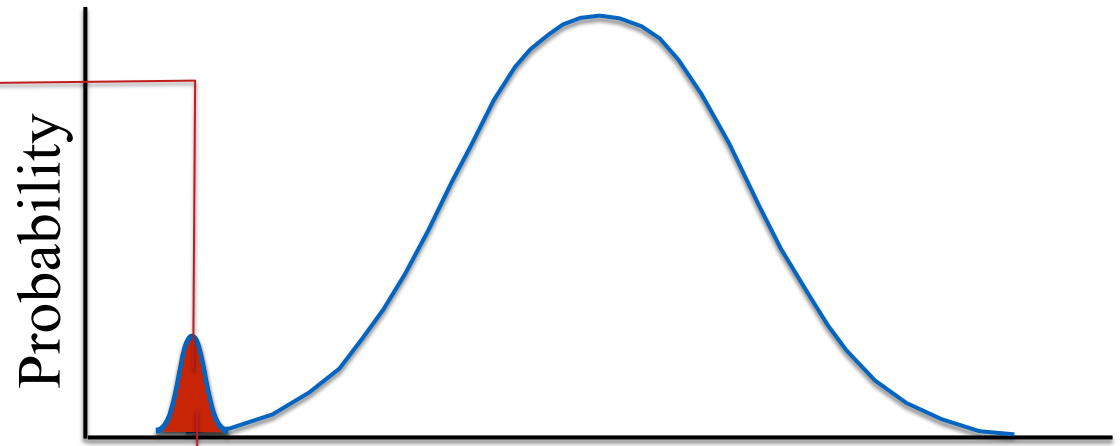


p-value histograms with & without significant events (I)

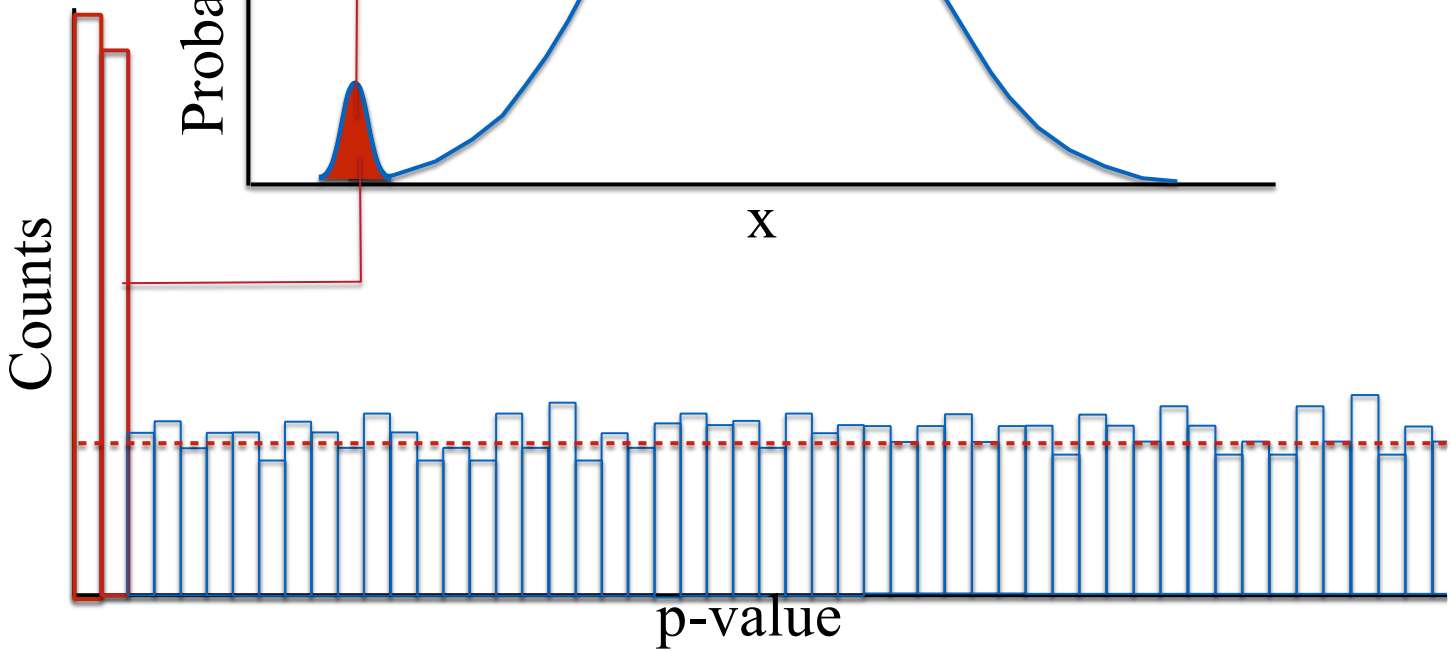
(A) No significant events.
q ~ 1



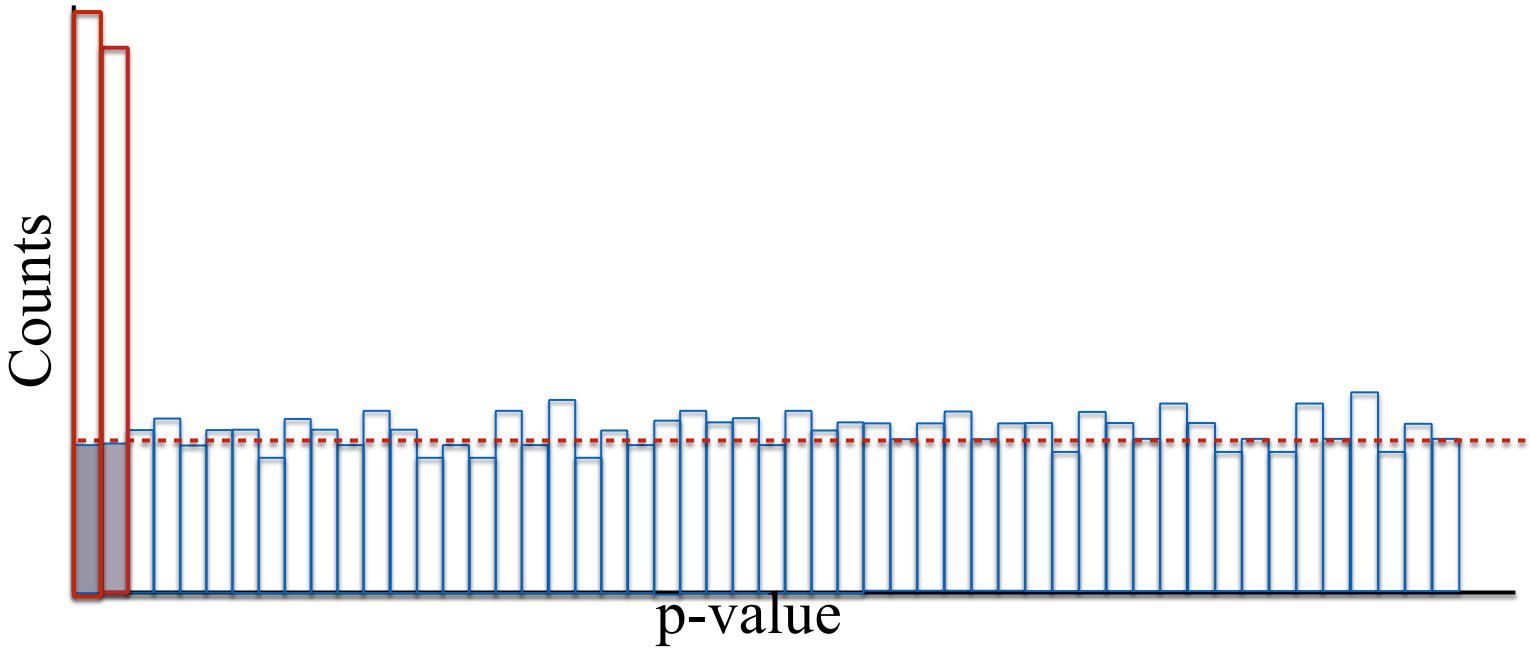
(B) Significant tests/events (red) with very small x.



(C) Large number of sinificant events.
q <<1



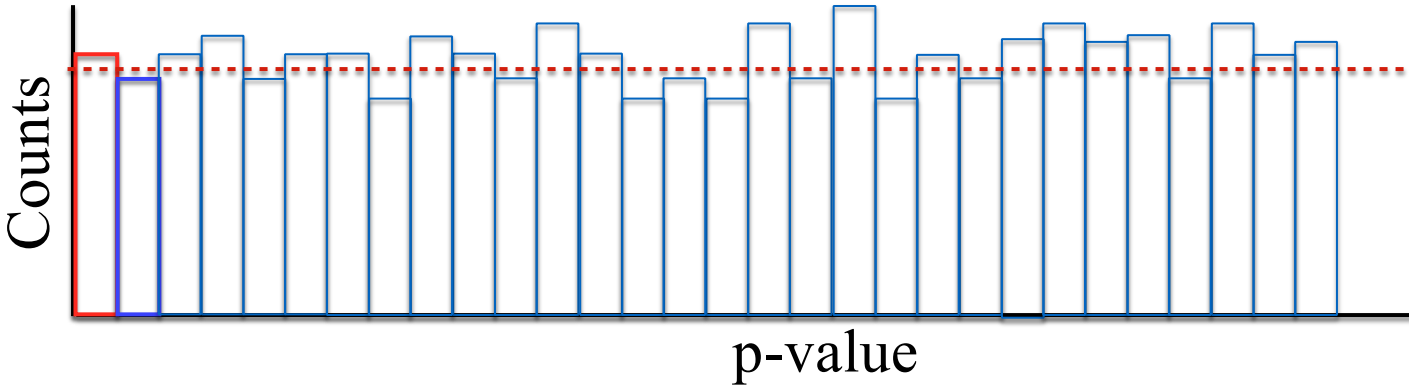
q-value



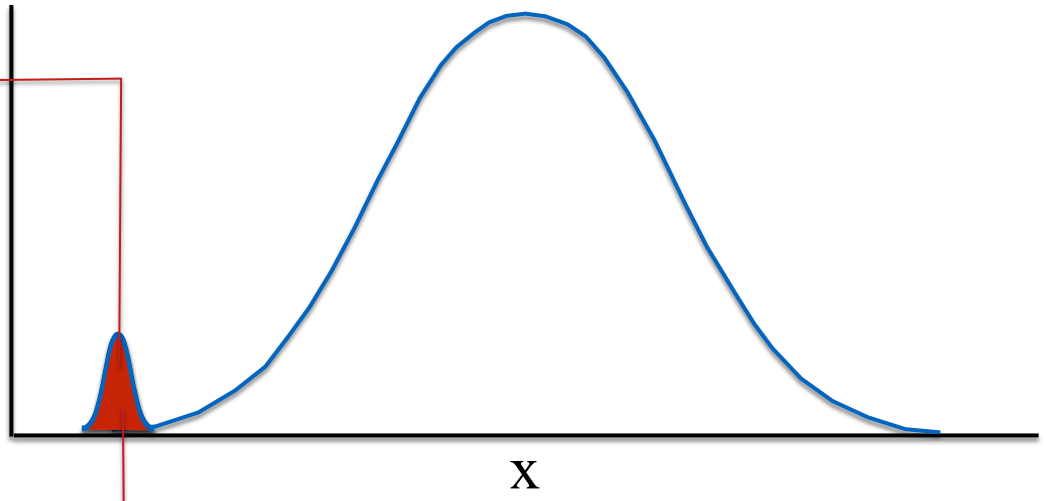
- Red events are the significant or positive events/tests (because they have, say, p< 0.05).
- Among the red events, the gray events are expected from the null theorem. They are likely false events. These are call false positives
- q-value = #of false positives/#of significant tests

p-value histograms with & without significant events (II)

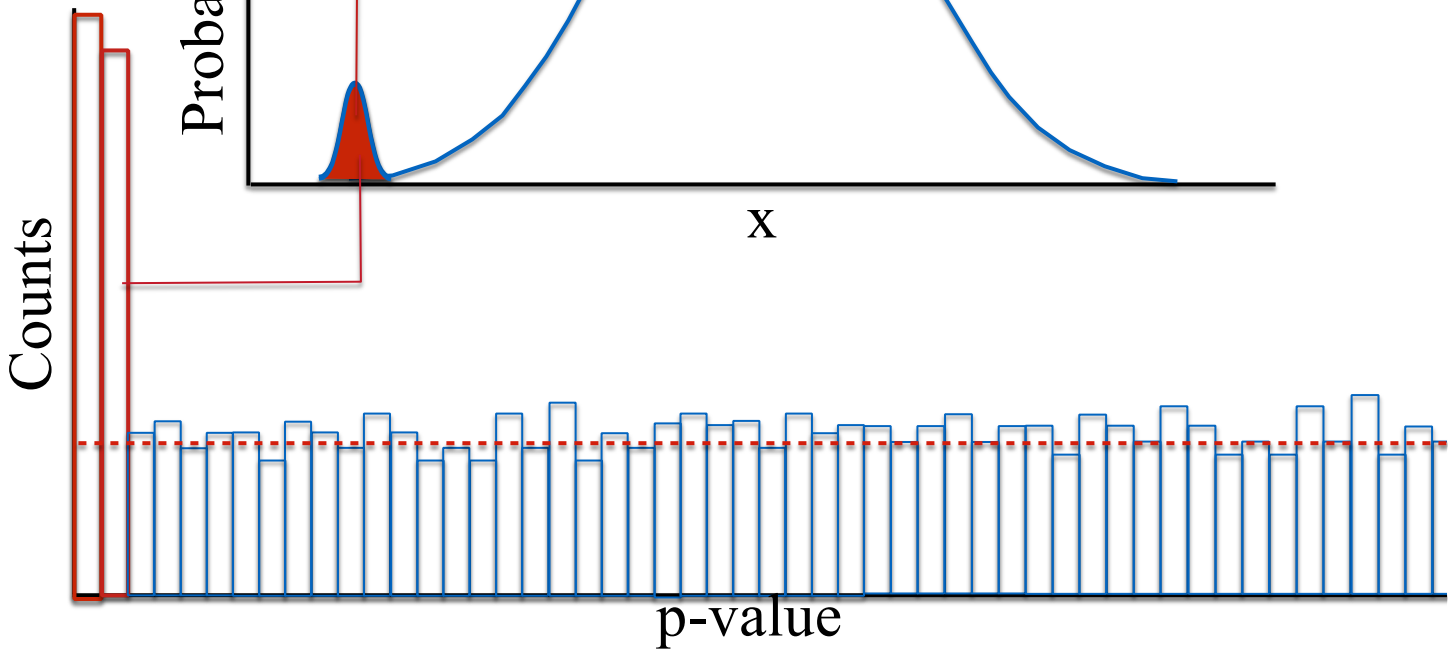
(A) Histogram of significant tests has small p-value, but null tests with same p-value has same count, hence tests are likely false positives.



(B) Significant tests/events (red) with very small x.



(C) Histogram of p-value for significant "red" events/tests is much higher than background, or average histogram for null tests. Hence some red events are likely true positives



Summary

- Null hypothesis is assumed for control group (nothing special); leads to null tests
- Sample group is for testing the Alternative hypothesis
- Positives are significant tests that the researcher identifies as supporting the alternative hypothesis (cannot be explained by null hypothesis)
- p-value is the probability a test is explained by the null hypothesis; minimum false positive rate.
- q-value is the proportion of significant tests that are false positives (null tests, or events due to null hypothesis); minimum false discovery rate (FDR)